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ORIGINAL ARTICLE

Moving towards the New International Study Group for Pancreatic Surgery (ISGPS) definitions in pancreaticoduodenectomy: a comparison between the old and new

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Abstract

Background: The International Study Group for Pancreatic Surgery (ISGPS) has proposed several definitions for postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and post-pancreatectomy haemorrhage (PPH). We assessed the effects of implementing these definitions on predicting outcomes.

Methods: A database of 77 patients who underwent pancreaticoduodenectomy between January 2005 and December 2009 was analysed. Morbidities were defined and classified using the ISGPS definitions and recalculated based on the definitions adopted by our institution ('Old' definitions) prior to the implementation of ISGPS definitions. Data for the two groups were then compared.

Results: The morbidity rate rose to 70.1% from 27.2% when ISGPS rather than Old definitions were used to define morbidities ($P < 0.001$). Incidences of DGE, POPF and PPH were 20.7%, 39.0% and 10.4%, respectively. Rates of DGE and POPF were significantly higher according to ISGPS definitions than to Old definitions (20.7% vs. 5.2% [$P = 0.001$] and 39.0% vs. 15.6% [$P = 0.004$], respectively). According to the ISGPS definitions, all of the 12 additional patients with DGE and 12 of the 18 additional patients with POPF had grade A morbidities. Patients with ISGPS-defined morbidity had a longer intensive care unit (ICU) stay, longer postoperative stay and longer total stay ($P = 0.030$, $P = 0.007$ and $P = 0.001$, respectively).

Conclusions: The morbidity rate more than doubled when ISGPS definitions were applied (an additional 42.9% of patients demonstrated morbidities). The majority of patients with DGE and POPF had grade A morbidities. The ISGPS definitions correlate well with ICU stay, postoperative stay and total length of stay.

Keywords

pancreaticoduodenectomy, Whipple operation, International Study Group for Pancreatic Surgery, delayed gastric emptying, postoperative pancreatic fistula, post-pancreatectomy haemorrhage

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Introduction

Over the last three decades, many centres have reported improved mortality rates in pancreaticoduodenectomy (PD), but morbidity rates remain high.[1–14] The wide variation in definitions for the various complications that may occur following pancreatic surgery has made comparison across different institutions difficult.[1,15–34] The International Study Group for Pancreatic Surgery (ISGPS) has proposed definitions and classifications for the common morbidities that occur after pancreatic surgery, namely, postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and post-pancreatectomy haemorrhage (PPH).[15,35,36] The aim of this study was to assess the effects on predicting outcomes of implementing the ISGPS definitions compared with the classification system used in this institution previously.

Materials and methods

A prospective database of all patients who underwent PD in our institution between January 2005 and December 2009 was

Table 1 International Study Group for Pancreatic Surgery grading of delayed gastric emptying after pancreatic surgery

DGE grade	NGT required	Unable to tolerate solid oral intake at:	Vomiting/gastric distension	Use of prokinetics
A	4–7 days or reinsertion after PoD 3	PoD 7	Yes/no	Yes/no
B	8–14 days or reinsertion after PoD 7	PoD 14	Yes	Yes
C	>14 days or reinsertion after PoD 14	PoD 21	Yes	Yes

DGE, delayed gastric emptying; NGT, nasogastric tube; PoD, postoperative day.
To exclude mechanical causes of abnormal gastric emptying, the patency of either the gastrojejunostomy or the duodenojejunostomy should be confirmed by endoscopy or upper gastrointestinal gastrographin series.
Adopted from Wente *et al*.[15]

analysed retrospectively. The new ISGPS guidelines to define and classify postoperative morbidities in pancreatic surgery were adopted in early 2006. Morbidity rates in the same cohort of patients were then recalculated using the systems of classifying DGE, POPF and PPH that had been in use locally prior to the implementation of the ISGPS definitions ('Old' definitions). Patients defined as having suffered morbidity by either classification were then identified. Outcomes measured were postoperative intensive care unit (ICU) stay, high-dependency unit (HDU) stay, length of hospital stay (LoS) and total length of stay (the sum of the stay from initial admission and any readmissions within 30 days of discharge). The two systems of classification were then compared to assess if the ISGPS definitions related to LoS parameters better than the definitions used in the previous classification system.

Data were analysed using SPSS Version 15.0 (SPSS, Inc., Chicago, IL, USA) and STATA Version 9.2 (StataCorp LP, College Station, TX, USA). Statistical significance was assumed at a *P*-value of <0.05. McNemar's test was used to cross-tabulate nominal data and the Mann–Whitney test was used for non-parametric continuous parameters.

The preoperative selection and workup of patients undergoing PD have been described previously.[37] Operative techniques for PD, including the classical Whipple procedure and pylorus-preserving PD have been reported previously.[38] The choice of the type of pancreatic-enteric anastomosis is based on the surgeon's preference. In general, hepatopancreatobiliary (HPB) surgeons choose to perform pancreaticojejunostomy (PJ), whereas upper gastrointestinal tract (UGI) surgeons prefer pancreaticogastrostomy.

A standard pancreatic surgery care pathway for postoperative management in the wards was applied since 2005. Surgery was performed by one of five surgeons (three HPB and two UGI surgeons) during the study period. A single dose of 200 mcg of subcutaneous sandostatin was administered during pancreatic transaction. Subcutaneous sandostatin was then continued for 1 week postoperatively at a dose established by the consistency of the pancreatic tissue as assessed during surgery. If the pancreas was soft or the pancreatic duct measured < 3 mm, 200 mcg was administered at 8-h intervals; otherwise 100 mcg was administered at 8-h intervals.[39] In the immediate postoperative period, patients were maintained on a nil-by-mouth regime in which a nasogastric tube (NGT) was used to facilitate passive drainage and aspiration at 4-h intervals. Patients were allowed non-milk feeds if their nasogastric output was < 100 ml on postoperative day (PoD) 1 and the NGT was removed on PoD 2 if output remained at < 100 ml. Feeding was graduated as tolerated. In general, by PoD 3 or 4, patients had started on a solid diet.

All complications were documented clearly and graded according to the ISGPS grading system when applicable (Tables 1–3). The specific complications examined include DGE, POPF and PPH.

Grade A DGE does not lead to any marked change in management other than for minor disturbances that occur during the return to intake of solid food.[15] Grade A POPF has no clinical impact and requires little change in management or deviation from the normal clinical pathway.[36] For the purposes of this study, grade A DGE and POPF are therefore referred to as clinically insignificant morbidities.

Prior to the definitions proposed by the ISGPS, morbidities were defined according to a different system of classification. This is compared with the ISGPS definitions in Table 4.

Perioperative mortality was defined as in-hospital death or death within 30 days of surgery.

Results

Demography

A total of 77 patients underwent PD during the study period, 40 of whom were male. Demographics, comorbidities and histology data are shown in Table 5.

Overall, 46 patients (59.7%) underwent a pylorus-preserving PD and the rest underwent a classical Whipple procedure. Pancreaticojejunostomy anastomosis was performed in 63 (81.8%) patients and pancreaticogastrostomy was carried out in the rest. The median duration of surgery was 580 min (range: 245–945 min). Median estimated blood loss was 1000 ml (range: 300–6000 ml). The median quantity of blood transfused was 2 units (range: 1–4 units).

Median postoperative stay and total LoS were 10 days (range: 5–137 days) and 15 days (range: 5–150 days), respectively. Median ICU stay was 1 day (range: 0–28 days) and median HDU stay was 3 days (range: 0–12 days). One patient had a long ICU stay of 28

Table 2 International Study Group for Pancreatic Surgery grading of postoperative pancreatic fistula after pancreatic surgery

	Grade A	Grade B	Grade C
Clinical conditions	Well	Often well	Appearing ill
Specific treatment[a]	No	Yes/no	Yes
US/CT (if obtained)	Negative	Negative/positive	Positive
Persistent drainage (after 3 weeks)[b]	No	Usually yes	Yes
Re-operation	No	No	Yes
Death related to POPF	No	No	Possibly yes
Signs of infections	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/no	Yes/no

[a]Partial (peripheral) or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analogue and/or minimal invasive drainage.
[b]With or without a drain *in situ*.
US, ultrasonography; CT, computed tomography; POPF, postoperative pancreatic fistula.
Adopted from Bassi *et al*.[36]

Table 3 International Study Group for Pancreatic Surgery grading of post-pancreatectomy haemorrhage after pancreatic surgery

Grade	Time of onset, location, severity and clinical impact of bleeding		Clinical condition	Diagnostic consequence	Therapeutic consequence
A	Early, intra- or extraluminal, mild		Well	Observation, blood count, US and, if necessary, CT	No
B	Early, intra- or extraluminal, severe	Later, intra- or extraluminal, mild[a]	Often well/intermediate, very rarely life-threatening	Observation, blood count, US, CT, angiography, endoscopy[b]	Transfusion of fluid-blood, intermediate care unit (or ICU), therapeutic endoscopy,[b] embolization, relaparotomy for early PPH
C		Late, intra- or extraluminal, severe	Severely impaired, life-threatening	Angiography, CT, endoscopy[b]	Localization of bleeding, angiography and embolization, (endoscopy[b]) *or* relaparotomy, ICU

[a]Late, intra- or extraluminal, mild bleeding may not be immediately life-threatening to the patient but may be a warning sign of later severe haemorrhage ('sentinel bleed') and is therefore grade B.
[b]Endoscopy should be performed when signs of intraluminal bleeding are present (melaena, haematemesis or blood loss via nasogastric tube).
US, ultrasonography; CT, computed tomography; ICU, intensive care unit; PPH, post-pancreatectomy haemorrhage.
Adopted from Wente *et al*.[35]

Table 4 Comparison of 'Old' and International Study Group for Pancreatic Surgery (ISGPS) definitions

Morbidity	Old definition used prior to ISGPS implementation	ISGPS definition
DGE	NGT required beyond PoD 7 Failure to tolerate solid diet before PoD 14	NGT required beyond PoD 3 Failure to tolerate solid diet before PoD 7
POPF	Clinically significant pancreatic leak with persistent pancreatic fluid drainage or intra-abdominal collection requiring percutaneous drainage, subsequently proven to be rich in amylase (>3 × serum amylase)	Abdominal drain output of any measurable volume of drain fluid on or after PoD 3 with an amylase content >3 × upper normal serum value
PPH	All cases of postoperative haemorrhage	All cases of postoperative haemorrhage

DGE, delayed gastric emptying; POPF, postoperative pancreatic fistula; PPH, post-pancreatectomy haemorrhage; NGT, nasogastric tube; PoD, postoperative day.

days after developing severe pneumonia with Type II respiratory failure and a burst abdomen postoperatively.

Median ICU, HDU and postoperative stays and total LoS in patients with and without morbidities were compared using the ISGPS and Old definitions. No differences were seen in ICU stay, HDU stay, postoperative stay or total LoS between patients with and without morbidities defined using the Old definitions. By contrast, patients with morbidities defined using the ISGPS definitions had significantly higher ICU stay, postoperative stay and total LoS (Table 6).

Overall morbidity rates according to the Old and the ISGPS definitions are compared in Table 7. The increase in DGE that emerged when ISGPS definitions were applied was caused solely by grade A DGE.

Table 5 Demographic data for patients in the present study ($n = 77$)

Age, years, median (range)	66 (29–83)
Ethnic group, *n* (%)	
Chinese	64 (83.1%)
Malay	3 (3.9%)
Indian	4 (5.2%)
Others	6 (7.8%)
Comorbidities, *n* (%)	
0	13 (16.9%)
1	15 (19.5%)
2	14 (18.3%)
>2	35 (45.5%)
ASA status, *n* (%)	
1	6 (7.8%)
2	34 (44.2%)
3	36 (46.8%)
4	1 (1.3%)
Histology, *n* (%)	
Adenocarcinoma	53 (68.8%)
Chronic pancreatitis	3 (3.9%)
Mucinous tumours	9 (11.7%)
Serous tumours	0
Villous adenomas	0
Others[a]	12 (15.6%)

[a]Includes histological diagnoses such as benign strictures, neuroendocrine tumours, inflammatory myofibroblastic tumours, solid cystic papillary neoplasms, sarcomas and cavernous lymphangiomas.
ASA, American Society of Anesthesiologists.

Using the ISGPS definition, an additional 18 patients were diagnosed with POPF. Of these, 12, five and one case were caused by grades A, B and C POPF, respectively.

The prevalence of PPH was 10.4% ($n = 8$); the same definition was employed both pre- and post-ISGPS implementation.

The overall mortality rate in the study population was 1.3% ($n = 1$).

Discussion

Studies on morbidities post-PD have been hampered by the lack of universally accepted definitions of the various postoperative occurrences, which has prevented the accurate comparison of surgical experiences among centres.[1,15–34,40,41] In a bid to overcome this problem, the ISGPS has proposed uniform definitions and classifications for the common postoperative morbidities in pancreatic surgery.[15,35,36] The aim of this study was to analyse the implementation of the ISGPS definitions and to determine whether they related better to outcomes than those previously used.

The morbidity rate in this cohort of patients more than doubled from 27.2% to 70.1% when ISGPS definitions rather than the previous (Old) definitions were used (i.e. an additional 42.9% of patients demonstrated morbidities). This reflected the more stringent ISGPS definitions for POPF and DGE. The high morbidity rate associated with the ISGPS definitions should be interpreted with caution as most of these morbidities were grade A cases that were not clinically significant; their exclusion resulted in a morbidity rate of only 31.2%. The inclusion of grade A morbidities in the ISGPS system of grading severity should be reviewed. A potential benefit of including grade A morbidities is that it heightens the index of suspicion in patients in whom they are identified, which may result in early intervention before the morbidity progresses to become clinically significant (grades B and C). However, their inclusion may also lead to a lowered threshold for instigating unnecessary investigations or procedures, such as computed tomography (CT) scans or drainage procedures. The clinical relevance and cost-effectiveness of considering grade A morbidities in clinical practice should be studied because their inclusion leads to an inflated morbidity rate with no proven clinical benefit. Nonetheless, compared with the previous system, the ISGPS definitions for post-PD morbidities appear to relate better to ICU stay, postoperative stay and total LoS. However, this improvement may in part reflect the larger number of patients defined as having complications, which increases the statistical power of detecting differences between those with and without morbidities.

Prior to the ISGPS era, rates of DGE in PD have been reported to vary from 20% to 60%.[12,42–46] In the current study, a further 15.5% of patients were found to have DGE when the ISGPS rather than the Old definition was used (20.7% vs. 5.2%; $P = 0.001$). This entire increase involved patients with grade A (clinically insignificant) DGE. The rate of DGE in the current study was lower than those reported in recently published studies using the ISGPS definition, in which DGE rates ranged from 33.3% to 44.5%.[16,47,48] By contrast with patients in a Korean study, which demonstrated an almost equal distribution between each grade of DGE,[16] patients with DGE in this study were predominantly grade A (12 of 16). This may be explained by an aggressive policy of feeding progression post-PD as the grading of DGE proposed by the ISGPS classification is dependent on the length of time until the patient first tolerates diet. A cautious approach in feeding progression may thus falsely inflate the incidence and severity of DGE. Thus, differing strategies in feeding progression may potentially contribute to differences in rates of DGE and may confound comparisons of DGE rates across institutions.

In the present cohort, a further 23.4% of patients were found to have POPF with the adoption of the ISGPS definition (39.0% vs. 15.6%; $P = 0.004$). Two-thirds of this increase was attributed to those with grade A POPF. The figures for POPF were comparable with those of other studies utilizing the ISGPS definition, in which rates of POPF varied from 10.2% to 50.0% and those of clinically significant POPF (grades B and C) ranged from 6.5% to 30.0%.[17,49–51] By contrast with other studies in which the majority of POPF was clinically significant, the vast majority of POPF cases in the current study were clinically insignificant (22 of 30).[17,50]

Table 6 Length of stay in patient groups defined according to 'Old' or International Study Group for Pancreatic Surgery (ISGPS) definitions

Hospital stay	With/without morbidity (Old definition) Length of stay, days, median (range)			With/without morbidity (ISGPS definition) Length of stay, days, median (range)		
	Morbidity	No morbidity	*P*-value	Morbidity	No morbidity	*P*-value
ICU stay	1.0 (0–28)	1.0 (0–4)	0.252	1.5 (0–28)	1.0 (0–3)	0.030[a]
HDU stay	2.5 (1–10)	3.0 (0–12)	0.962	3.0 (0–6)	3.0 (1–12)	0.369
Overall postoperative stay	11.5 (7–137)	10.0 (5–83)	0.560	12.0 (5–137)	9.0 (5–22)	0.007[a]
Total stay	17.0 (8–150)	13.5 (5–86)	0.184	18.0 (7–150)	10.0 (5–23)	0.001[a]

[a]Statistically significant at $P < 0.05$.
ICU, intensive care unit; HDU, high-dependency unit.

Table 7 Morbidity rates using 'Old' vs. International Study Group for Pancreatic Surgery (ISGPS) definitions in all patients ($n = 77$)

	Old definition	ISGPS definition	Increase	*P*-value
Overall morbidity	27.2% ($n = 21$)	70.1% ($n = 54$)	42.9% ($n = 33$)	$P < 0.001$[a]
Specific morbidity				
DGE	5.2% ($n = 4$)	20.7% ($n = 16$)	15.5% ($n = 12$)	$P = 0.001$[a]
POPF	15.6% ($n = 12$)	39.0% ($n = 30$)	23.4% ($n = 18$)	$P = 0.004$[a]
PPH	10.4% ($n = 8$)	10.4% ($n = 8$)	0	$P = 1.000$

[a]Statistically significant at $P < 0.05$.
DGE, delayed gastric emptying; POPF, postoperative pancreatic fistula; PPH, post-pancreatectomy haemorrhage.

This may reflect a higher threshold for ordering imaging modalities post-PD compared with other institutions as health care costs in our nation are predominantly self-funded. Thus, fewer clinically insignificant peripancreatic collections requiring CT scans for diagnosis (grade B POPF) are detected, with the result that more POPF patients are classified as having grade A rather than grade B POPF. Thus, different patterns in resource utilization may potentially influence the severity grading of POPF.

Conclusions

Using the ISGPS definitions of post-PD morbidities caused the morbidity rate in this study cohort to more than double from 27.2% to 70.1% (i.e. an additional 42.9% of patients demonstrated morbidities). The majority of patients with DGE and POPF had grade A morbidities. The ISGPS definitions correlate well with ICU stay, postoperative stay and total LoS.

Conflicts of interest

None declared.

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